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Mr. Stephen Johnson, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building, 1101 -A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Public Comments on the HPV Challenge Program Test Plan for the Cobalt Stearate and Fatty acids, Tall Oil, Cobalt Salts Category by Members of the Metal Carboxylates Coalition (OM Group, Inc., The Shepherd Chemical Company and Troy Corporation).

The following comments on the HPV Challenge Program test plan for the Cobalt Stearate and Fatty Acids, Tall Oil, Cobalt Salts Category by members of the Metal Carboxylates Coalition (OM Group, Inc. and The Shepherd Chemical Company) are submitted on behalf of People for the Ethical Treatment of Animals, the Physicians Committee for Responsible Medicine, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

In our August 15, 2006 submission, we requested that EPA reopen the comment period for the metal carboxylates test plans, since, as a result of breaking up the category, the numbers of animals to be used has greatly increased and there are a number of serious scientific and animal welfare concerns that need to be addressed. This is the fifth set of comments that we have submitted on the new individual test plans.

The sponsoring companies are proposing to conduct the following tests on animals: acute oral LD_{50} tests for both cobalt stearate and fatty acids, tall oil, cobalt salts; a combined repeated dose test with repro/developmental screen, OECD 422, for cobalt stearate; and an acute fish toxicity test for cobalt stearate. If conducted, these tests will cause the suffering and death of approximately 815 animals.

This test plan violates the following terms of the October 1999 agreement among EPA, industry, and health, animal protection, and environmental organizations, as well as the December 2000 *Federal Register* notice reconfirming that agreement:

2. Participants shall maximize the use of existing and scientifically adequate data to minimize further testing.

3. Participants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships.

Cobalt carboxylates are used as oxidative polymerization catalysts in many industries. Other uses include oxygen scavenger plastics and as adhesion promoters in tire manufacturing. The sponsoring companies note that metal carboxylates readily dissociate into free metal and free acid. The proportion of dissociated salt is dependent on the pH, and the dissociation constant (pKa) is the pH at which 50% dissociation occurs. The pKa values for each category member as determined in studies conducted by the Metal Carboxylates Coalition are reported to be 7.5 for cobalt stearate and 5.82 for fatty acids, tall oil, cobalt salts. These values indicate that complete dissociation will occur at the physiologically relevant pH of the mammalian stomach (pH 1.2). The sponsoring companies conclude therefore, that when administered orally, the toxicity of these metal carboxylates is due to the independent action of the respective acid and the free cobalt ion. As a result, mammalian toxicity data for the free acids and free metal ion, or its simple metal salts, can serve as surrogate data for that of the respective metal carboxylates. In support of this conclusion, the work of Stopford, et al. (2003)[1] is cited to show that cobalt chloride is similar to, or more bioavailable than, the corresponding cobalt carboxylate salts, thus making the chloride a conservative surrogate in estimating bioavailability and toxicity of the dissociated metal ion.

An acute oral LD_{50} test is proposed for fatty acids, tall oil, cobalt salts. An acute oral LD_{50} test also appears to be proposed for cobalt stearate, since it is listed in the test plan summary and table. However, we note that this test is missing from the proposed test plan section. Reliable existing data for cobalt stearate are summarized from an acute mammalian toxicity study conducted for one of the sponsoring companies, The Shepherd Chemical Company. Surprisingly, no mention is made of these existing data in the test plan. Further, these data should satisfy the endpoint for the other category member, fatty acids, tall oil, cobalt salts, by read-across. In any case, it is difficult to understand how this exceptionally agonizing test could be proposed for both category members when reducing testing by read-across is the rationale for establishing categories of related chemicals to begin with.

Existing data is also summarized for the dissociation products, tall oil fatty acid and cobalt chloride. Although no existing data is summarized here for stearic acid, Chemtura Corporation recently summarized an acute oral toxicity study for stearic acid in their HPV Program test plan for barium stearate.[2] It should also be noted that stearic acid is the most common of the long-chain fatty acids and is labeled a "Generally Recognized as Safe (GRAS)" food additive by the Food and Drug Administration (FDA). As such, EPA recommends that HPV Program participants consider whether the data supporting FDA's conclusions make it unnecessary to proceed with further testing on animals. In its comments on the Aluminum Stearates Category, EPA notes that "under 40 CFR § 180.910, stearic acid is exempt from the requirement of tolerance (i.e. is designated as 'minimal risk'), obviating the need for further testing under that authority." In addition, stearic acid is already being sponsored in the HPV Program by the Aliphatic Acids Consortium of the Soap and Detergent Association. The theoretical discussion of metal carboxylates dissociation presented in the test plan and summarized above clearly shows that, under the conditions of the proposed test (i.e. oral administration), existing data for the dissociation products fully characterize the toxicity of the metal carboxylates in this category. If the existing data for cobalt stearate, cobalt chloride, stearic acid, and tall oil fatty acid, along with that supporting the FDA's GRAS determination for stearic acid, are perceived to be inadequate,

the sponsoring companies should, at a minimum, wait for stearic acid data generated by the Aliphatic Acids Consortium to be submitted before initiating new testing.

A combined repeated dose test with repro/developmental screen, OECD 422, is proposed for cobalt stearate. Existing repeated dose toxicity data are summarized for each category member's dissociation products, cobalt chloride, stearic acid and tall oil fatty acid. Existing repro/developmental data are summarized for tall oil fatty acid and cobalt chloride. Under the conditions of the proposed test, existing data for the dissociation products, along with category read-across for the cobalt stearate repro/developmental endpoints, satisfy the data requirements for both metal carboxylates in this category without the need for new testing. As with the proposed oral LD_{50} test mentioned above, if the existing data for the dissociation products, along with that supporting the FDA's GRAS determination for stearic acid, are perceived to be inadequate, the sponsoring companies should wait for stearic acid data generated by the Aliphatic Acids Consortium to be submitted before initiating new testing. Because the Metal Carboxylates Coalition submitted its original test plan in 2003, the sponsoring companies may be unaware that a similar approach, using existing data on dissociation products, was subsequently endorsed by the EPA and all stakeholders in 2004 for E. I. du Pont de Nemours & Company's test plan for triisopropylborate, a compound which breaks down to isopropanol and boric acid in water (see http://www.epa.gov/oppt/chemrtk/triprobt/c14841tc.htm). This approach has been used in a number of other test plans as well in which compounds dissociate at low pH and the toxicity data on the dissociation products has been used to meet the SIDS requirements.

A fish acute toxicity test is proposed for cobalt stearate. No reliable ecotoxicity data for aquatic plants or invertebrates exist for cobalt stearate. The fish test is intended to show whether exposure to cobalt stearate will result in large-scale fish death thereby predicting economic loss and ecologic damage. If this exposure kills the food on which fish subsist, it could deplete fish populations even without direct fish toxicity. Since the toxicity of cobalt stearate to aquatic plants and invertebrates is still unknown, tests on fish are premature. In addition, ECOSAR and non-animal ecotoxicity tests, such as the DarT test[3] and TETRATOX test[4] should be considered. In those cases for which fish acute toxicity tests are still perceived to be required, ECVAM's Ecotoxicology Task Force recently published an evaluation of a fish acute threshold (step-down) test concept with the potential to reduce the number of fish used in ecotoxicity testing by 53.6%-71.2%.[5]

In summary, while the sponsoring companies summarize existing data for members of this category and their dissociation products and present a convincing theoretical argument for the use of dissociation product data to serve as surrogates for those of the respective metal carboxylates, they nevertheless fail to use this analysis to minimize animal testing as specified by the EPA in both the October 1999 letter to chemical sponsors and the December 2000 *Federal Register* notice on the HPV program. Instead, the sponsoring companies propose additional testing for acute mammalian, repeated dose, and repro/developmental toxicity endpoints without justification. We urge the sponsoring companies and the EPA to reject these proposed tests as well as to consider the applicability of the suggested alternatives to the fish acute toxicity test.

Sincerely,

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Research & Investigations

[1] Stopford W., Turner J, Cappellini D, and Brock T. 2003. Bioaccessibility testing of cobalt compounds. J. Environ. Monit. 5(4): 675-680.
[2] Clayton, GD., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Witey & Sons Inc., 1993-1994. 3568. Cited in BiblioLine
[3] Nagel, R. 2002. DarT: the embryo test with the zebrafish *Danio rerio*: A general model in ecotoxicology and toxicology. *ALTEX* 19 (Suppl. 1), 38-48.
[4] Schultz, T.W. 1997. TETRATOX *Tetrahymena pyriformis* population growth impairment endpoint: A surrogate for fish lethality. *Toxicological Methods* 7, 289-309.
[5] Jerama, S., et al. 2005. A strategy to reduce the use of fish in acute ecotoxicity testing of new chemical substances notified in the European Union. *Regulatory Toxicology and Pharmacology* 42, 218–224.